(a) contacting said compound composition with a population of from about 10 to 1000 small non-mammalian multi-cellular organisms having a rapid generation time and differentiated organs and tissues; and

(b) determining the effect of said compound composition on said non-mammalian multi-cellular organisms;

wherein each of said compound compositions is selected from the group consisting of: known pharmacologically active compounds, chemical analogs thereof, and candidate pharmacologically active agents.

15. (Amended) The method according to Claim 12, wherein at least 1000 candidate compound compositions are tested simultaneously.

16. (Amended) The method according to Claim 12, wherein said multi-cellular organism is an insect.

REMARKS

The above amendments to Claims 1, 6, 15 and 16 correct clerical errors in drafting the claims. As such, the above amendments introduce no new matter and their entry by the Examiner is respectfully requested. Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Claims 1, 6, 9-10 and 15-16 were objected to for various issues. In view of the above amendments to these claims, this rejection may be withdrawn.

Claims 3 and 4 were rejected under 35 U.S.C. § 112, 2nd ¶ for two issues.

First, the Examiner asserts that the phrase "rapid generation time" is indefinite because this term is not described sufficiently in the specification, i.e., "the specification does not provide a standard for ascertaining the requisite degree." The specification states as follows:

> The multi-cellular organisms employed in the subject HTS methods are also characterized by having a rapid generation time. A rapid generation time is important to maintain the breeding colony plus supply enough organisms that will **be prolific enough to produce on average at least about 100 progeny per day**, which is the minimum requirement for high throughput sceening. Page 5, lines 2 to 6.

The above discussion provides those of skill in the art with clear parameters as to what is meant by an organism that has rapid generation time, i.e., such an organism is one that produces on average at least about 100 progeny per day. As such, this term is not indefinite to those of skill in the art when read in light of the specification.

The Examiner has also rejected the term "small" of claim 4 for the same reasons, i.e., the specification assertedly does not provide guidance as to what is meant by small. However, the specification states at page 4, lines 24 to page 5 line 1:

> As the organisms employed in the subject methods are multi-cellular, they include differentiated tissues and organs. They are further characterized by being relatively small, where by small is meant at least about .001 g, usually at least about .01 g and more usually at least about .1 g, where the average mass of each organism in the plurality may be as great as 10 g or greater, but typically does not exceed about 100 g and usually does not exceed about 1,000 g.

As such, the specification provides one of skill in the art with clear parameters as to what is and what is not meant by small.

In view of the above remarks, it is respectfully submitted that Claims 3 and 4 are not indefinite for use of the terms "rapid generation time" and "small," and therefore the rejection of these claims under 35 U.S.C. § 112, 2nd ¶ may be withdrawn.

Claims 1-7, 10-13 and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Wasserkort. However, Wasserkort is screening volatile organics which are not "pharmacologically active compounds, chemical analogs thereof, and new candidate pharmacologically active agents." The

pending claims in question are limited to those in which the screened compounds are "pharmacologically active compounds, chemical analogs thereof, and new candidate pharmacologically active agents." Furthermore, Claims 12 to 16 are even further distinguished from Wasserkort in that these claims are directed to a method of screening for a candidate compounds antitoxin activity, where the candidate compound and a known toxin are both contacted with the organism. Nothing in Wasserkort teaches or suggests such an assay, as Wasserkort says nothing about testing antitoxin activity of candidate compounds. As such, Wasserkort does not anticipate the claimed methods of Claims 1-7, 10-13 and 16 and this rejection may be withdrawn.

Claims 1-7, 10-13 and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Lynch. The assay disclosed in Lynch is not a toxicity assay but instead is a teratogenicity assay. Lynch states that the purpose of the work was to "create a new, rapid and economical bioassay useful in screening for potential developmental toxicants." Lynch also teaches that the pregnant females are the animals exposed to the toxins and the effect of this parental exposure on the phenotypes of the offspring is that which is evaluated. This description of the assay methods is in complete agreement with the accepted definition of teratogenicity tests. Enclosed with this response please find an excerpt from Fundamental Toxicology for Chemists, which excerpt provides definitions for both teratogenicity and toxicity.

In contrast, a toxicity test is one that looks at the effect of a compound on the immediate organism to which it is exposed, and not the offspring of the exposed organism.

Furthermore, Claims 12 to 16 are even further distinguished from Lynch in that these claims are directed to a method of screening for a candidate compound's antitoxin activity, where the candidate compound and a known toxin are both contacted with the organism. Nothing in Lynch teaches or suggests such an assay, as Lynch says nothing about testing antitoxin activity of candidate compounds.

Because the present claims are directed to methods of performing a toxicity assay, or an antitoxin assay, and not to methods of performing a teratogenicity assay, Lynch fails to anticipate the claimed methods and the rejection of Claims 1-7, 10-13 and 16 have been rejected under 35 U.S.C. § 102(b) over Lynch may be withdrawn.

Claims 8-9 and 14-15 have been rejected under 35 U.S.C. § 103(a) as obvious over either Wasserkort or Lynch for the asserted reason that the only difference between the claims and the cited references is the number of compounds tested, which is asserted to be an obvious difference. However, as pointed out above, Wasserkort is not directed to pharmaceutical agents but instead volatile organic alcohols and Lynch is a teratogenicity screen, not a toxicity screen. As such, both Lynch and Wasserkort fail to teach or suggest the elements of the present claims and this rejection may be withdrawn.

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 8.9.01

By: _____
Bret E. Field
Registration No. 37,620

- Excerpt from Fundamental Toxicology for Chemists

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\tosk\004\response to office action of 5-9-01.doc

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A high throughput toxicology screening method in which at least 10 different compound compositions are simultaneously assayed for toxicity, said method comprising:

simultaneously assaying at least 10 different compound compositions for toxicity, wherein each of said at least 10 different compound compositions is assayed for toxicity by:

(a) contacting said compound composition with a plurality of non-mammalian multi-cellular organisms; and

(b) determining the effect of said compound composition on said non-mammalian multi-cellular organisms;

wherein each of said compound compositions is selected from the group consisting of~~:~~ known pharmacologically active compounds, chemical analogs thereof, and new candidate pharmacologically active agents.

6. (Amended) A high throughput toxicology screening method in which at least 10 different compound compositions are simultaneously assayed for toxicity, said method comprising:

simultaneously assaying at least 10 different compound compositions for toxicity, wherein each of said at least 10 different compound compositions is assayed for toxicity by:

(a) contacting said compound composition with a population of from about 10 to 1000 small non-mammalian multi-cellular organisms having a rapid generation time and differentiated organs and tissues; and

(b) determining the effect of said compound composition on said non-mammalian multi-cellular organisms;

wherein each of said compound compositions is selected from the group consisting of~~:~~ known pharmacologically active compounds, chemical analogs thereof, and candidate pharmacologically active agents.

15. (Amended) The method according to ~~Claim 6~~ Claim 12, wherein at least 1000 candidate compound compositions are tested simultaneously.

16. (Amended) The method according to ~~Claim 6~~ Claim 12, wherein said multi-cellular organism is an insect.